

IN THE SPECIFICATION

Please amend the Specification as indicated below.

Following the title and prior to the first paragraph, please insert the following new paragraph:

-- This Application is a U.S. national stage filing under 35 U.S.C. 371 of PCT/EP2003/014542 filed December 18, 2003, from which priority is claimed. --

Please replace the paragraph at page 7, lines 25-32, with the following paragraph:

-- The SP-B precursor (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 1) comprises the "mature peptide" (79 amino acids) flanked by a 200 amino acid N-terminal propeptide (including a 23 amino acid signal peptide) and a 102 amino acid C-terminal propeptide, respectively. The fragment comprising the N-terminal propeptide and the mature peptide (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 2) was demonstrated to be necessary and sufficient for both correct folding and transport of SP-B. The removal of the N-terminal propeptide and release of mature SP-B (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 3) occurs in type II alveolar cells. So far, it has not been possible to produce mature SP-B in any conventional cell culture systems, such as HeLa cells or CHO cells (cf. above). --

Please replace the sentence at page 7, lines 34-35, with the following sentence:

-- Thus, in a preferred embodiment of the invention, the surfactant protein component of the fusion protein is the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 2. --

Please replace the text at page 8, line 1, through page 9, line 5, with the following text:

-- In an alternative preferred embodiment of the invention, the surfactant protein component of the fusion protein is the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 3.

The post-translational processing of the SP-C precursor (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 8) is very similar to that of SP-B. Mature SP-C (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 10), a small protein of only 35 amino acids, is produced by subsequent cleavage of the C- and N-terminal propeptide, respectively (reviewed in [9,10,12]).

In another preferred embodiment of the invention, the surfactant protein precursor of the fusion protein is SP-C (the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 9).

In a further preferred embodiment of the invention, the surfactant protein component of the fusion protein is the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 10.

A preferred fusion partner for SP-B and SP-C, respectively, with regard to an object of the invention, i.e. lysis of surfactant containing fibrin clots, is urokinase-plasminogen activator (u-PA), since it is the predominant plasminogen activator in the alveolar space. Urokinase-plasminogen activator is synthesized as a 411 amino acid precursor protein as well, which is termed single-chain u-PA (or pro-urokinase; the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 4). Cleavage between Lys-158 and Ile-159 results in the formation of high molecular weight two-chain u-PA (HMW-u-PA). Further processing by cleavage between Lys-135 and Lys-136 generates low molecular weight two-chain u-PA (LMW-u-PA; the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 5), which is reported to have a similar enzymatic activity as the high molecular weight form. The two chains of the protein are connected by a disulfide-bridge between Cys-148 and Cys-279. However, it is possible to use in the present invention any proteinaceous plasminogen activator or fragment or mutant thereof as long as this polypeptidic molecule has plasminogen activator activity.

In a further preferred embodiment of the invention, the plasminogen activator of the

fusion protein is the LMW-u-PA polypeptide the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 5.

Most preferably, the fusion protein of the invention is a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 6 and SEQ ID NO: 7 comprising chimeras of the SP-B precursor (SP-B_{ΔC}) and LMW-u-PA, which are referred to as SPUC1A and SPUC1B, respectively (see also Fig. 1A and 1B).

In another particular preferred embodiment of the invention, the fusion protein is a polypeptide encoded by a nucleic acid sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 13 comprising chimeras of the mature SP-B (SP-B_{mature}) and LMW-u-PA, which are referred to as SPUC@C and SPUC3B, respectively (see also Fig. 1C and 1D).

Also preferred is a fusion protein comprising tissue-plasminogen activator (t-PA; the polypeptide encoded by the nucleic acid sequence shown as SEQ ID NO: 11) as the plasminogen activator component. --